

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 3 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) – May 28, 2002]

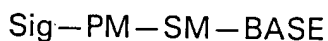
**KINDLY AMEND THE ABOVE-IDENTIFIED APPLICATION AS FOLLOWS:**

**In The Claims:**

Please enter new claims 576-825 as follows:

---

1 ~~576.~~ An oligo- or polydeoxyribonucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polydeoxyribonucleotide comprising at least one modified nucleotide having the formula



N<sup>1</sup> wherein PM is a phosphate moiety, SM is a sugar moiety and BASE is a base moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, said PM being attached to SM, said BASE being attached to SM, and Sig being covalently attached to PM directly or through a chemical linkage, said Sig comprising a non-polypeptide, non-radioactive label moiety which can be directly or indirectly detected when attached to PM or when said modified nucleotide is incorporated into said oligo- or polydeoxyribonucleotide or when said oligo- or polydeoxyribonucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof.

577. The oligo- or polydeoxyribonucleotide of claim 576, wherein said Sig is or renders the nucleotide or the oligo- or polydeoxyribonucleotide self-signaling or self-indicating or self-detecting.

Dean L. Engelhardt, et al.

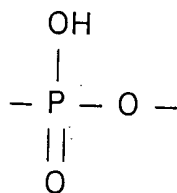
Serial No.: 08/479,997

Filed: June 7, 1995

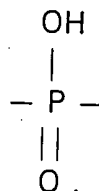
Page 4 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

<sup>2</sup>  
~~578~~. The oligo- or polydeoxyribonucleotide of claim ~~576~~<sup>1</sup>, wherein said Sig moiety comprises at least three carbon atoms.

<sup>3</sup>  
~~579~~. The oligo- or polydeoxyribonucleotide of claim ~~576~~<sup>1</sup>, wherein said covalent attachment is selected from the group consisting of



and



<sup>4</sup>  
~~580~~. The oligo- or polydeoxyribonucleotide of claim ~~576~~<sup>1</sup>, wherein said chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

SUB  
D<sup>1</sup>  
~~581~~. The oligo- or polydeoxyribonucleotide of claim 576, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the  $\alpha$ -position relative to the point of attachment to the nucleotide, a  $-\text{CH}_2\text{NH}-$  moiety, or both.

<sup>6</sup>  
~~582~~. The oligo- or polydeoxyribonucleotide of claim ~~576~~<sup>1</sup>, wherein said chemical linkage comprises an allylamine group.

Dean L. Engelhardt, et al.

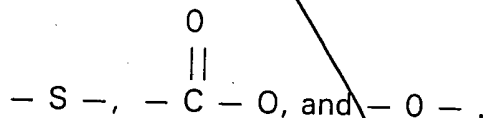
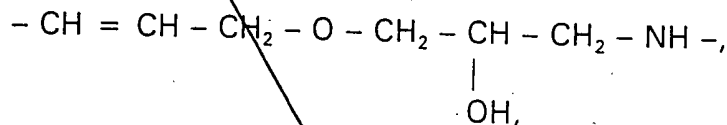
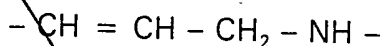
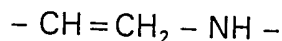
Serial No.: 08/479,997

Filed: June 7, 1995

Page 5 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) – May 28, 2002]

SUB  
02

583. The oligo- or polydeoxyribonucleotide of claim 576, wherein said chemical linkage comprises or includes an olefinic bond at the  $\alpha$ -position relative to the point of attachment to the nucleotide, or any of the moieties:



N<sup>1</sup>  
CDU#

8  
584. The oligo- or polydeoxyribonucleotide of claim 576, wherein said chemical linkage of Sig includes a glycosidic linkage moiety.

9  
585. The oligo- or polydeoxyribonucleotide of claim 576, wherein said PM is monophosphate, a diphosphate or a triphosphate and said Sig moiety is covalently attached to said PM through a phosphorus atom or phosphate oxygen.

10  
586. The oligo- or polydeoxyribonucleotide of claim 576, wherein Sig comprises a component selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, a metal-containing component, a fluorescent component, a chemiluminescent component, a chromogenic component or a combination of any of the foregoing.

11  
587. The oligo- or polydeoxyribonucleotide of claim 586, wherein said electron dense component comprises ferritin.

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 6 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

<sup>12</sup>  
~~588~~. The oligo- or polydeoxyribonucleotide of claim ~~586~~<sup>10</sup>, wherein said magnetic component comprises magnetic oxide.

<sup>13</sup>  
~~589~~. The oligo- or polydeoxyribonucleotide of claim ~~588~~<sup>12</sup>, wherein said magnetic oxide comprises ferric oxide.

N<sup>1</sup>  
C004.  
<sup>14</sup>  
~~590~~. The oligo- or polydeoxyribonucleotide of claim ~~586~~<sup>10</sup>, wherein said metal-containing component is catalytic.

<sup>15</sup>  
~~591~~. The oligo- or polydeoxyribonucleotide of claim ~~586~~<sup>10</sup>, wherein said fluorescent component comprises a member selected from the group consisting of fluorescein, rhodamine and dansyl.

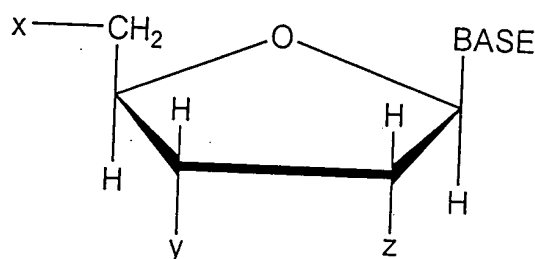
<sup>16</sup>  
~~592~~. The oligo- or polydeoxyribonucleotide of claim ~~576~~<sup>1</sup>, wherein said Sig moiety is attached to a terminal nucleotide in said oligo- or polydeoxyribonucleotide.

<sup>17</sup>  
~~593~~. The oligo- or polydeoxyribonucleotide of claim ~~592~~<sup>16</sup>, wherein the sugar moiety of said terminal nucleotide has a hydrogen atom at the 2' position thereof.

<sup>18</sup>  
~~594~~. The oligo- or polydeoxyribonucleotide of claim ~~592~~<sup>16</sup>, wherein the sugar moiety of said terminal nucleotide has oxygen atoms at each of the 2' and 3' positions thereof.

<sup>19</sup>  
~~595~~. The oligo- or polydeoxyribonucleotide of claim ~~576~~<sup>1</sup>, comprising at least one ribonucleotide.

20  
586. An oligo- or polydeoxyribonucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polydeoxyribonucleotide comprising at least one modified nucleotide having the structural formula:



N<sup>1</sup>  
CDU-4.  
wherein BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, and wherein BASE is attached to the 1' position of the pentose ring from the N1 position when BASE is a pyrimidine or from the N9 position when BASE is a purine or a deazapurine;

wherein x is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein y is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein z is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate; and

wherein Sig is covalently attached directly or through a chemical linkage to at least one phosphate selected from the group consisting of x, y, z, and a combination thereof, said Sig comprising a non-polypeptide, non-radioactive label moiety which can be directly or indirectly detected when so attached to said phosphate or when said modified nucleotide is incorporated into said oligo- or polydeoxyribonucleotide or when said oligo- or polydeoxyribonucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof.

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

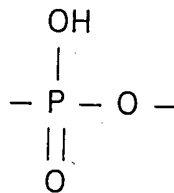
Filed: June 7, 1995

Page 8 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) – May 28, 2002]

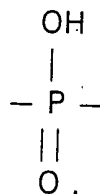
597. The oligo- or polydeoxyribonucleotide of claim 596, wherein said Sig is or renders the nucleotide or the oligo- or polydeoxyribonucleotide self-signaling or self-indicating or self-detecting.

598. The oligo- or polydeoxyribonucleotide of claim 596, wherein said Sig moiety comprises at least three carbon atoms.

599. The oligo- or polydeoxyribonucleotide of claim 596, wherein said covalent attachment is selected from the group consisting of



and



600. The oligo- or polydeoxyribonucleotide of claim 596, wherein said chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 9 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

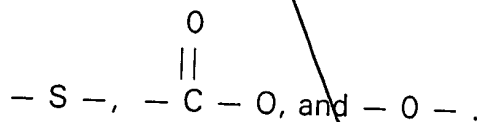
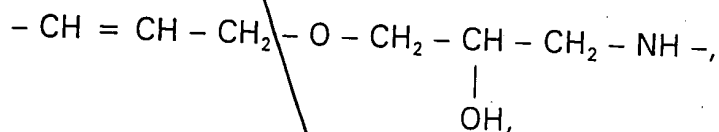
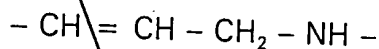
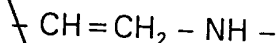
SUB  
03

601. The oligo- or polydeoxyribonucleotide of claim 596, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the  $\alpha$ -position relative to the point of attachment to the nucleotide, a  $-\text{CH}_2\text{NH}-$  moiety, or both.

25 20  
602. The oligo- or polydeoxyribonucleotide of claim ~~596~~, wherein said chemical linkage comprises an allylamine group.

N'  
COND.

603. The oligo- or polydeoxyribonucleotide of claim 596, wherein said chemical linkage comprises or includes an olefinic bond at the  $\alpha$ -position relative to the point of attachment to x, y or z, or any of the moieties:



27 20  
604. The oligo- or polydeoxyribonucleotide of claim ~~596~~, wherein said chemical linkage of Sig includes a glycosidic linkage moiety.

28 20  
605. The oligo- or polydeoxyribonucleotide of claim ~~596~~, wherein said x and y each comprise a member selected from the group consisting of a monophosphate, a diphosphate and a triphosphate and said Sig moiety is covalently attached to either or both of said x and y through a phosphorus atom or phosphate oxygen.

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 10 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

<sup>29</sup>  
~~606~~. The oligo- or polydeoxyribonucleotide of claim ~~596~~<sup>29</sup>, wherein Sig comprises a component selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, a metal-containing component, a fluorescent component, a chemiluminescent component, a chromogenic component or a combination of any of the foregoing.

<sup>30</sup>  
~~607~~. The oligo- or polydeoxyribonucleotide of claim ~~606~~<sup>29</sup>, wherein said electron dense component comprises ferritin.

N<sup>1</sup>  
cont.  
<sup>31</sup>  
~~608~~. The oligo- or polydeoxyribonucleotide of claim ~~606~~<sup>29</sup>, wherein said magnetic component comprises magnetic oxide.

<sup>32</sup>  
~~609~~. The oligo- or polydeoxyribonucleotide of claim ~~608~~<sup>31</sup>, wherein said magnetic oxide comprises ferric oxide.

<sup>33</sup>  
~~610~~. The oligo- or polydeoxyribonucleotide of claim ~~606~~<sup>29</sup>, wherein said metal-containing component is catalytic.

<sup>34</sup>  
~~611~~. The oligo- or polydeoxyribonucleotide of claim ~~606~~<sup>29</sup>, wherein said fluorescent component comprises a member selected from the group consisting of fluorescein, rhodamine and dansyl.

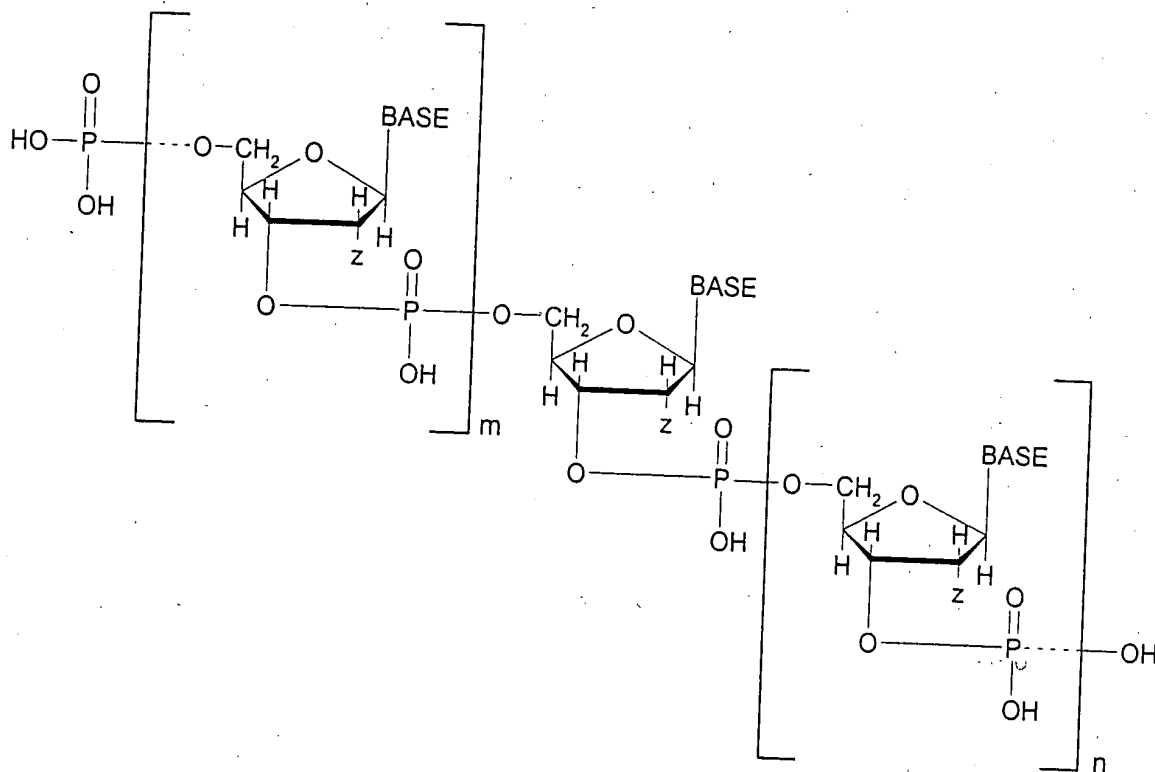
<sup>35</sup>  
~~612~~. The oligo- or polydeoxyribonucleotide of claim ~~596~~<sup>20</sup>, wherein said Sig moiety is attached to a terminal nucleotide in said oligo- or polydeoxyribonucleotide.



~~614~~<sup>37</sup>. The oligo- or polydeoxyribonucleotide of claim ~~612~~<sup>35</sup>, wherein both y and z of said terminal nucleotide comprise an oxygen atom at each of the 3' and 2' positions thereof, respectively.

~~38~~  
615. The oligo- or polydeoxyribonucleotide of claim ~~596~~<sup>20</sup>, comprising at least one ribonucleotide.

<sup>39</sup>  
~~616~~. The oligo- or polydexoyribonucleotide of claim ~~596~~<sup>20</sup>, having the structural formula:



wherein m and n represent integers from 0 up to about 100,000, and wherein said Sig. moiety is attached to at least one of the phosphate moieties in said structural formula.

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 12 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

40

617. An oligo- or polynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polynucleotide comprising at least one modified nucleotide having the formula

Sig - PM - SM - BASE

N<sup>1</sup>  
cont.

wherein PM is a phosphate moiety, SM is a sugar moiety and BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, said PM being attached to SM, said BASE being attached to SM, and Sig being covalently attached to PM directly or via a chemical linkage, said Sig comprising a non-polypeptide, non-radioactive label moiety which can be directly or indirectly detected when attached to PM or when said modified nucleotide is incorporated into said oligo- or polynucleotide, or when said oligo- or polynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof, provided that when said oligo- or polynucleotide is an oligoribonucleotide or a polyribonucleotide, and when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2',3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide.

618. The oligo- or polynucleotide of claim 617, wherein said Sig is or renders the nucleotide or the oligo- or polynucleotide self-signaling or self-indicating or self-detecting.

41

40  
619. The oligo- or polynucleotide of claim 617, wherein said Sig moiety comprises at least three carbon atoms.

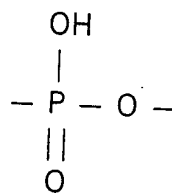
Dean L. Engelhardt, et al.

Serial No.: 08/479,997

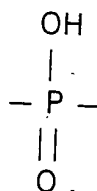
Filed: June 7, 1995

Page 13 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

42/ 620. The oligo- or polynucleotide of claim 617, wherein said covalent attachment is selected from the group consisting of



and



43 621. The oligo- or polynucleotide of claim 617, wherein said chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

622. The oligo- or polynucleotide of claim 617, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the  $\alpha$ -position relative to the point of attachment to the nucleotide, a  $-\text{CH}_2\text{NH}-$  moiety, or both.

45 623. The oligo- or polynucleotide of claim 617, wherein said chemical linkage comprises an allylamine group.

Dean L. Engelhardt, et al.

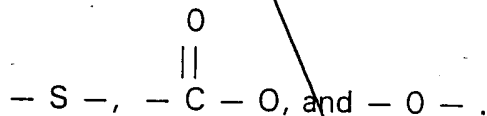
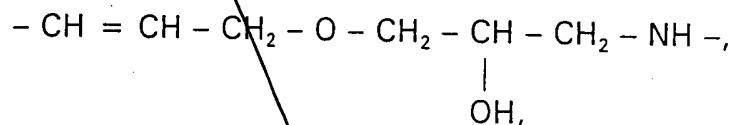
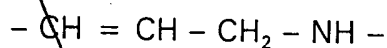
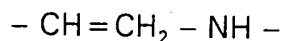
Serial No.: 08/479,997

Filed: June 7, 1995

Page 14 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) – May 28, 2002]

543  
06  
N'  
cont.

624. The oligo- or polynucleotide of claim 617, wherein said chemical linkage comprises or includes an olefinic bond at the  $\alpha$ -position relative to the point of attachment to the nucleotide, or any of the moieties:



47

625. The oligo- or polynucleotide of claim 617, wherein said chemical linkage of Sig includes a glycosidic linkage moiety.

48

40

626. The oligo- or polynucleotide of claim 617, wherein said PM is a monophosphate, a diphosphate or a triphosphate and said Sig moiety is covalently attached to said PM through a phosphorus atom or a phosphate oxygen.

49

40

627. The oligo- or polynucleotide of claim 617, wherein Sig comprises a component selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, a metal-containing component, a fluorescent component, a chemiluminescent component, a chromogenic component or a combination of any of the foregoing.

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 15 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

~~50~~ 628. The oligo- or polynucleotide of claim ~~49~~ 627, wherein said electron dense component comprises ferritin.

~~51~~ 629. The oligo- or polynucleotide of claim ~~49~~ 627, wherein said magnetic component comprises magnetic oxide.

~~52~~ 630. The oligo- or polynucleotide of claim ~~51~~ 629, wherein said magnetic oxide comprises ferric oxide.

~~53~~ 631. The oligo- or polynucleotide of claim ~~49~~ 627, wherein said metal-containing component is catalytic.

~~54~~ 632. The oligo- or polynucleotide of claim ~~49~~ 627, wherein said fluorescent component comprises a member selected from the group consisting of fluorescein, rhodamine and dansyl.

~~55~~ 633. The oligo- or polynucleotide of claim ~~40~~ 617, wherein said Sig moiety is attached to a terminal nucleotide in said oligo- or polynucleotide.

~~56~~ 634. The oligo- or polynucleotide of claim ~~55~~ 633, wherein the sugar moiety of said terminal nucleotide has a hydrogen atom at the 2' position thereof.

~~57~~ 635. The oligo- or polynucleotide of claim ~~55~~ 633, wherein the sugar moiety of said terminal nucleotide has an oxygen atom at each of the 2' and 3' positions thereof.

Dean L. Engelhardt, et al.

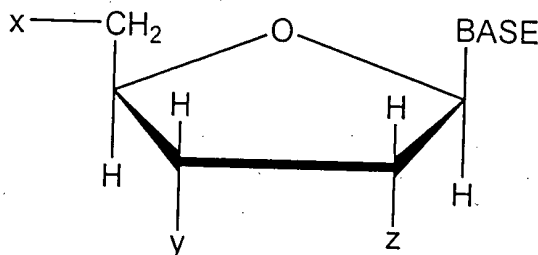
Serial No.: 08/479,997

Filed: June 7, 1995

Page 16 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

<sup>58</sup>  
~~636~~. The oligo- or polynucleotide of claim <sup>47</sup>~~617~~, comprising at least one deoxyribonucleotide.

<sup>59</sup>  
~~637~~. An oligo- or polynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polynucleotide comprising at least one modified nucleotide having the structural formula:



wherein BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, and wherein BASE is attached to the 1' position of the pentose ring from the N1 position when BASE is a pyrimidine or from the N9 position when BASE is a purine or a deazapurine;

wherein x is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein y is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein z is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate; and

wherein Sig is covalently attached directly or through a chemical linkage to at least one phosphate selected from the group consisting of x, y and z, and a combination thereof, said Sig comprising a non-polypeptide, non-radioactive label moiety which can be directly or indirectly detected when so attached to said

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

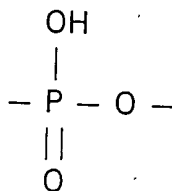
Page 17 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

N<sup>1</sup>  
C804  
phosphate or when said modified nucleotide is incorporated into said oligo- or polynucleotide, or when said oligo- or polynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof, provided that when said oligo- or polynucleotide is an oligoribonucleotide or a polyribonucleotide and when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2',3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide.

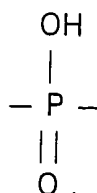
638. The oligo- or polynucleotide of claim 637, wherein said Sig is or renders the nucleotide or the oligo- or polynucleotide self-signaling or self-indicating or self-detecting.

60  
639. The oligo- or polynucleotide of claim 59, wherein said Sig moiety comprises at least three carbon atoms.

61  
640. The oligo- or polynucleotide of claim 59, wherein said covalent attachment is selected from the group consisting of



and



Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

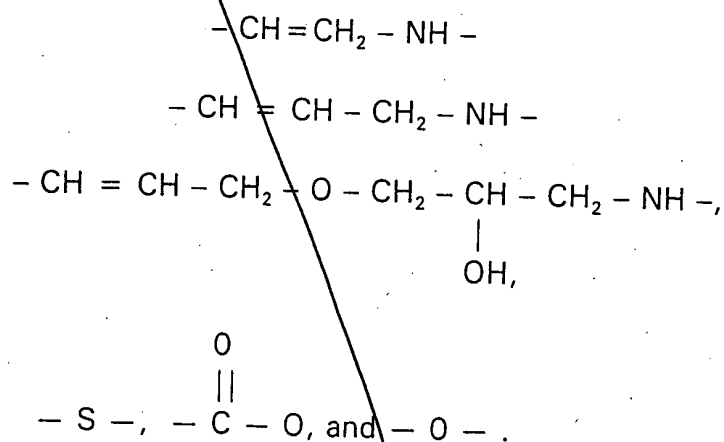
Page 18 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

<sup>62</sup>  
~~641.~~ The oligo- or polynucleotide of claim ~~637~~<sup>59</sup>, wherein said chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

SUB  
07 → 642. The oligo- or polynucleotide of claim 637, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the α-position relative to the point of attachment to the nucleotide, a -CH<sub>2</sub>NH- moiety, or both.

N<sup>1</sup>  
COOH <sup>64</sup>  
~~643.~~ The oligo- or polynucleotide of claim ~~637~~<sup>59</sup>, wherein said chemical linkage comprises an allylamine group.

644. The oligo- or polynucleotide of claim 637, wherein said chemical linkage comprises or includes an olefinic bond at the α-position relative to x, y or z, or any of the moieties:



<sup>66</sup>  
~~645.~~ The oligo- or polynucleotide of claim ~~637~~<sup>59</sup>, wherein said chemical linkage of Sig includes a glycosidic linkage moiety.



Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 19 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

<sup>67</sup>  
~~646~~. The oligo- or polynucleotide of claim ~~637~~<sup>59</sup>, wherein said x and y each  
comprise a member selected from the group consisting of a monophosphate, a  
diphosphate and a triphosphate and Sig moiety is covalently attached to either or  
both of said x and y through a phosphorus atom or a phosphate oxygen.

<sup>68</sup>  
~~647~~. The oligo- or polynucleotide of claim ~~637~~<sup>59</sup>, wherein Sig comprises a  
component selected from the group consisting of biotin, iminobiotin, an electron  
dense component, a magnetic component, a metal-containing component, a  
fluorescent component, a chemiluminescent component, a chromogenic component  
or a combination of any of the foregoing.

<sup>69</sup>  
~~648~~. The oligo- or polynucleotide of claim ~~647~~<sup>68</sup>, wherein said electron dense  
component comprises ferritin.

<sup>70</sup>  
~~649~~. The oligo- or polynucleotide of claim ~~647~~<sup>68</sup>, wherein said magnetic component  
comprises magnetic oxide.

<sup>71</sup>  
~~650~~. The oligo- or polynucleotide of claim ~~649~~<sup>70</sup>, wherein said magnetic oxide  
comprises ferric oxide.

<sup>72</sup>  
~~651~~. The oligo- or polynucleotide of claim ~~647~~<sup>68</sup>, wherein said metal-containing  
component is catalytic.

<sup>73</sup>  
~~652~~. The oligo- or polynucleotide of claim ~~647~~<sup>68</sup>, wherein said fluorescent  
component comprises a member selected from the group consisting of fluorescein,  
rhodamine and dansyl.

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 20 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

<sup>74</sup>  
~~653~~. The oligo- or polynucleotide of claim ~~637~~<sup>59</sup>, wherein said Sig moiety is  
attached to a terminal nucleotide in said oligo- or polynucleotide.

<sup>75</sup>  
~~654~~. The oligo- or polynucleotide of claim ~~653~~<sup>74</sup>, wherein z of said terminal  
nucleotide comprises a hydrogen atom at the 2' position thereof.

<sup>76</sup>  
~~655~~. The oligo- or polynucleotide of claim ~~653~~<sup>74</sup>, wherein both y and z of said  
terminal nucleotide comprise an oxygen atom at each of the 3' and 2'  
positions thereof, respectively.

<sup>77</sup>  
~~656~~. The oligo- or polynucleotide of claim ~~637~~<sup>59</sup>, comprising at least one  
deoxyribonucleotide.

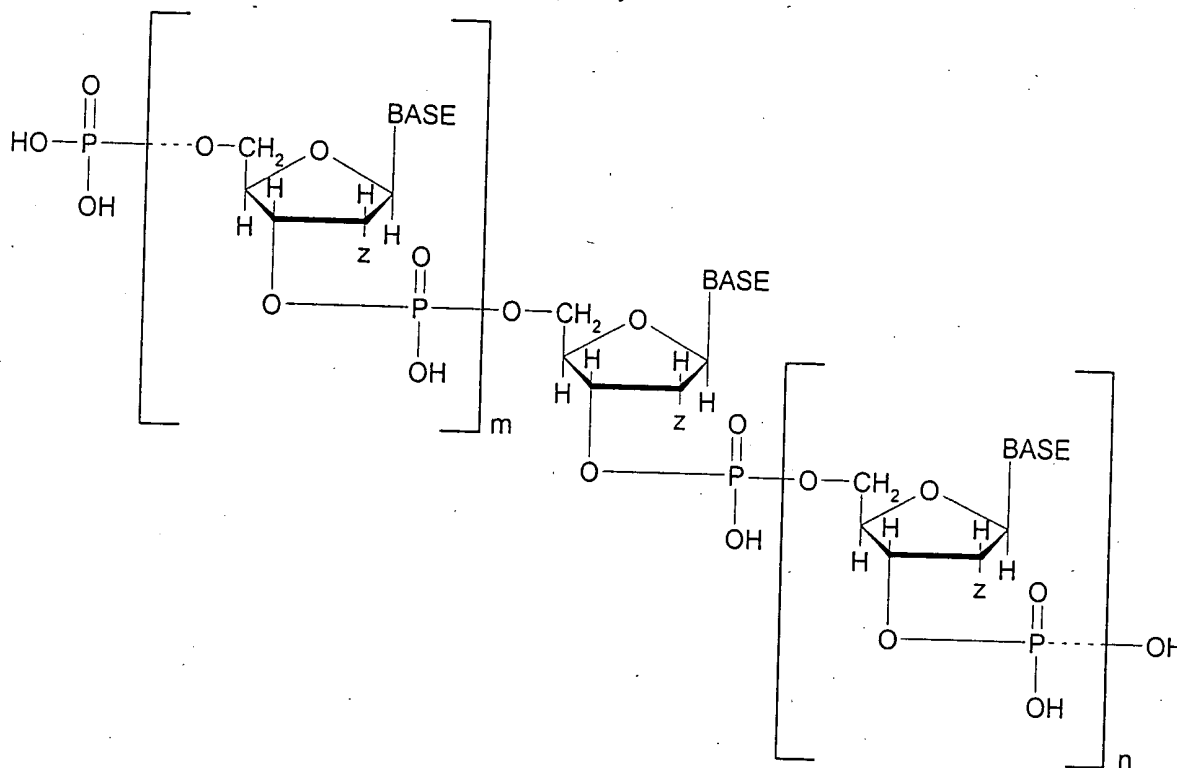
Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 21 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

<sup>78</sup>  
~~657~~. The oligo- or polynucleotide of claim <sup>59</sup>~~637~~, having the structural formula:



wherein m and n represent integers from 0 up to about 100,000, and wherein said Sig moiety is attached to at least one of the phosphate moieties in said structural formula.

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 22 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) – May 28, 2002]

79

658. An oligo- or polydeoxyribonucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polydeoxyribonucleotide comprising at least one modified nucleotide having the formula

Sig-PM-SM-BASE

N<sup>1</sup>  
const  
wherein PM is a phosphate moiety, SM is a sugar moiety and BASE is a base moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, said PM being attached to SM, said BASE being attached to SM, and Sig being covalently attached to PM directly or through a chemical linkage, said Sig comprising a non-radioactive label moiety which can be directly or indirectly detected when attached to PM or when said modified nucleotide is incorporated into said oligo- or polydeoxyribonucleotide or when said oligo- or polydeoxyribonucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof, and wherein Sig comprises biotin, iminobiotin, an electron dense component, a magnetic component, a metal-containing component, a fluorescent component, a chemiluminescent component, a chromogenic component or a combination of any of the foregoing.

659. The oligo- or polydeoxyribonucleotide of claim 658, wherein said Sig is or renders the nucleotide or the oligo- or polydeoxyribonucleotide self-signaling or self-indicating or self-detecting.

80

660. The oligo- or polydeoxyribonucleotide of claim 658, wherein said Sig moiety comprises at least three carbon atoms.

79

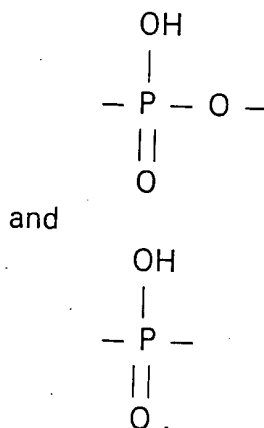
Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 23 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

~~81~~ 79  
661. The oligo- or polydeoxyribonucleotide of claim ~~658~~, wherein said covalent attachment is selected from the group consisting of



N<sup>1</sup>  
CD<sup>154</sup>  
~~82~~ 79  
662. The oligo- or polydeoxyribonucleotide of claim ~~658~~, wherein said chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

SWB  
D9  
~~663. The oligo- or polydeoxyribonucleotide of claim 658, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the  $\alpha$ -position relative to the point of attachment to the nucleotide, a -CH<sub>2</sub>NH- moiety, or both.~~

~~84~~ 79  
664. The oligo- or polydeoxyribonucleotide of claim ~~658~~, wherein said chemical linkage comprises an allylamine group.

Dean L. Engelhardt, et al.

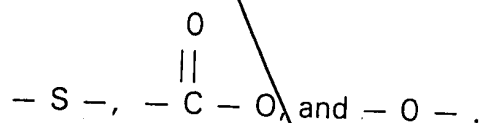
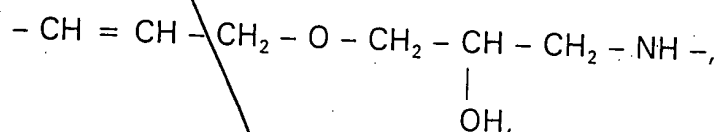
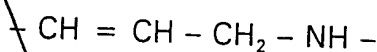
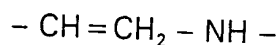
Serial No.: 08/479,997

Filed: June 7, 1995

Page 24 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) – May 28, 2002]

SUB  
610

665. The oligo- or polydeoxyribonucleotide of claim 658, wherein said chemical linkage comprises or includes an olefinic bond at the  $\alpha$ -position relative to the point of attachment to the nucleotide, or any of the moieties:



86  
666. The oligo- or polydeoxyribonucleotide of claim 658, wherein said chemical linkage of Sig includes a glycosidic linkage moiety. 79

87  
667. The oligo- or polydeoxyribonucleotide of claim 658, wherein said PM is monophosphate, a diphosphate or a triphosphate and said Sig moiety is covalently attached to said PM through a phosphorus atom or phosphate oxygen. 79

88  
668. The oligo- or polydeoxyribonucleotide of claim 658, wherein said electron dense component comprises ferritin. 79

89  
669. The oligo- or polydeoxyribonucleotide of claim 658, wherein said magnetic component comprises magnetic oxide. 79

90  
670. The oligo- or polydeoxyribonucleotide of claim 658, wherein said magnetic oxide comprises ferric oxide. 79

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 25 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) – May 28, 2002]

~~91~~ ~~79~~  
~~671~~. The oligo- or polydeoxyribonucleotide of claim ~~658~~, wherein said metal-containing component is catalytic.

~~92~~ ~~79~~  
~~672~~. The oligo- or polydeoxyribonucleotide of claim ~~658~~, wherein said fluorescent component comprises a member selected from the group consisting of fluorescein, rhodamine and dansyl.

~~93~~ ~~79~~  
~~673~~. The oligo- or polydeoxyribonucleotide of claim ~~658~~, wherein said Sig moiety is attached to a terminal nucleotide in said oligo- or polydeoxyribonucleotide.

N<sup>1</sup>  
CDS<sup>4</sup>  
~~94~~ ~~93~~  
~~674~~. The oligo- or polydeoxyribonucleotide of claim ~~673~~, wherein the sugar moiety of said terminal nucleotide has a hydrogen atom at the 2' position thereof.

~~95~~ ~~93~~  
~~675~~. The oligo- or polydeoxyribonucleotide of claim ~~673~~, wherein the sugar moiety of said terminal nucleotide has oxygen atoms at each of the 2' and 3' positions thereof.

~~96~~ ~~79~~  
~~676~~. The oligo- or polydeoxyribonucleotide of claim ~~658~~, comprising at least one ribonucleotide.

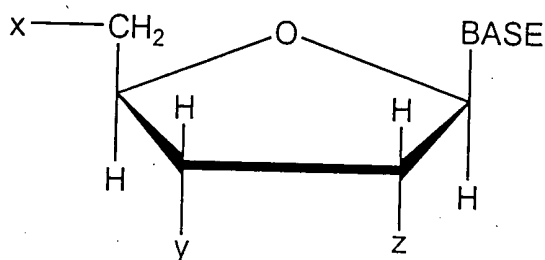
Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 26 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

97  
677. An oligo- or polydeoxyribonucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polydeoxyribonucleotide comprising at least one modified nucleotide having the structural formula:



N<sup>1</sup>  
cost.  
wherein BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, and wherein BASE is attached to the 1' position of the pentose ring from the N1 position when BASE is a pyrimidine or from the N9 position when BASE is a purine or a deazapurine;

wherein x is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein y is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein z is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate; and

wherein Sig is covalently attached directly or through a chemical linkage to at least one phosphate selected from the group consisting of x, y, z, and a combination thereof, said Sig comprising a non-radioactive label moiety which can be directly or indirectly detected when so attached to said phosphate or when said modified nucleotide is incorporated into said oligo- or polydeoxyribonucleotide or when said oligo- or polydeoxyribonucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof, wherein Sig comprises biotin,



Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

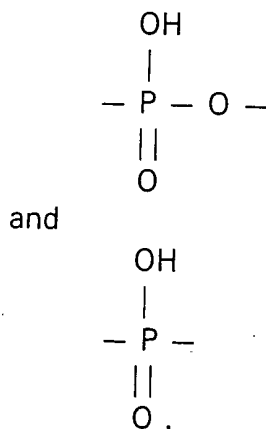
Page 27 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) – May 28, 2002]

iminobiotin, an electron dense component, a magnetic component, a metal-containing component, a fluorescent component, a chemiluminescent component, a chromogenic component or a combination of any of the foregoing.

678. The oligo- or polydeoxyribonucleotide of claim 677, wherein said Sig is or renders the nucleotide or the oligo- or polydeoxyribonucleotide self-signaling or self-indicating or self-detecting.

98  
N<sup>1</sup> 679. The oligo- or polydeoxyribonucleotide of claim 677, wherein said Sig moiety comprises at least three carbon atoms.

99  
680. The oligo- or polydeoxyribonucleotide of claim 677, wherein said covalent attachment is selected from the group consisting of



100  
681. The oligo- or polydeoxyribonucleotide of claim 677, wherein said chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 28 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

SUB  
011

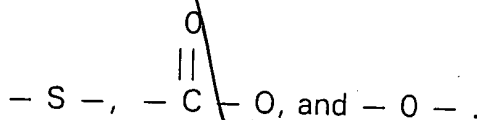
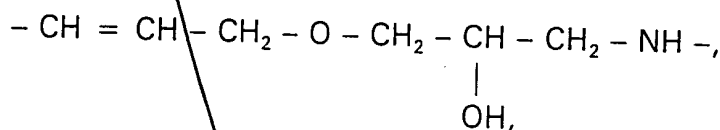
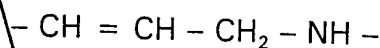
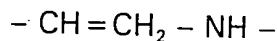
682. The oligo- or polydeoxyribonucleotide of claim 677, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the  $\alpha$ -position relative to the point of attachment to the nucleotide, a  $-\text{CH}_2\text{NH}-$  moiety, or both.

102 97

683. The oligo- or polydeoxyribonucleotide of claim 677, wherein said chemical linkage comprises an allylamine group.

N'  
COO<sup>+</sup>

684. The oligo- or polydeoxyribonucleotide of claim 677, wherein said chemical linkage comprises or includes an olefinic bond at the  $\alpha$ -position relative to the point of attachment to x, y or z, or any of the moieties:



104 97

685. The oligo- or polydeoxyribonucleotide of claim 677, wherein said chemical linkage of Sig includes a glycosidic linkage moiety.

105 97

686. The oligo- or polydeoxyribonucleotide of claim 677, wherein said x and y each comprise a member selected from the group consisting of a monophosphate, a diphosphate and a triphosphate and said Sig moiety is covalently attached to either or both of said x and y through a phosphorus atom or phosphate oxygen.

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 29 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

<sup>106</sup>  
~~687~~. The oligo- or polydeoxyribonucleotide of claim ~~677~~<sup>97</sup>, wherein said electron dense component comprises ferritin.

<sup>107</sup>  
~~688~~. The oligo- or polydeoxyribonucleotide of claim ~~677~~<sup>97</sup>, wherein said magnetic component comprises magnetic oxide.

N<sup>1</sup>  
CD 4.  
<sup>108</sup>  
~~689~~. The oligo- or polydeoxyribonucleotide of claim ~~688~~<sup>107</sup>, wherein said magnetic oxide comprises ferric oxide.

<sup>109</sup>  
~~690~~. The oligo- or polydeoxyribonucleotide of claim ~~677~~<sup>97</sup>, wherein said metal-containing component is catalytic.

<sup>110</sup>  
~~691~~. The oligo- or polydeoxyribonucleotide of claim ~~677~~<sup>97</sup>, wherein said fluorescent component comprises a member selected from the group consisting of fluorescein, rhodamine and dansyl.

<sup>111</sup>  
~~692~~. The oligo- or polydeoxyribonucleotide of claim ~~677~~<sup>97</sup>, wherein said Sig moiety is attached to a terminal nucleotide in said oligo- or polydeoxyribonucleotide.

<sup>112</sup>  
~~693~~. The oligo- or polydeoxyribonucleotide of claim ~~692~~<sup>111</sup>, wherein z of said terminal nucleotide comprises a hydrogen atom at the 2' position thereof.

<sup>113</sup>  
~~694~~. The oligo- or polydeoxyribonucleotide of claim ~~692~~<sup>111</sup>, wherein both y and z of said terminal nucleotide comprise an oxygen atom at each of the 3' and 2' positions thereof, respectively.

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

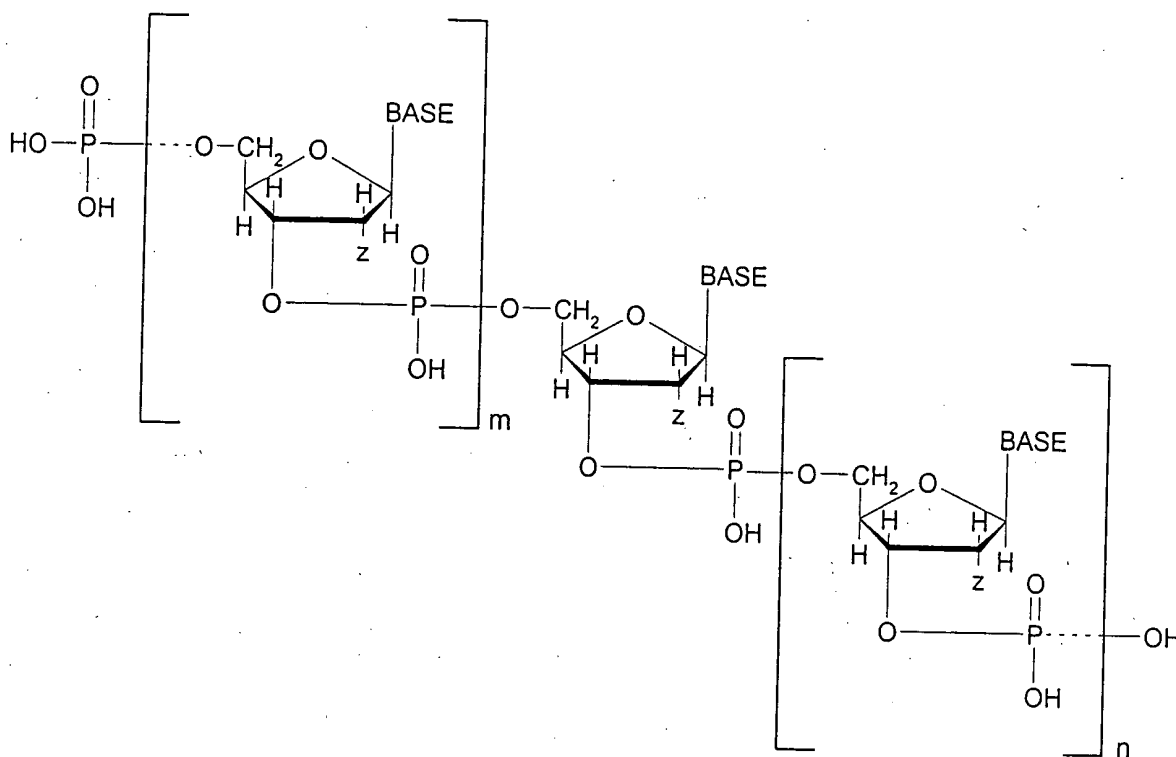
Page 30 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

114

695. The oligo- or polydeoxyribonucleotide of claim ~~67~~<sup>97</sup>, comprising at least one ribonucleotide.

115

696. The oligo- or polydeoxyribonucleotide of claim ~~67~~<sup>97</sup>, having the structural formula:



wherein m and n represent integers from 0 up to about 100,000, and wherein said Sig moiety is attached to at least one of the phosphate moieties in said structural formula.

Dean L. Engelhardt, et al.

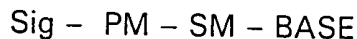
Serial No.: 08/479,997

Filed: June 7, 1995

Page 31 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) – May 28, 2002]

116

~~697~~. An oligo- or polynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polynucleotide comprising at least one modified nucleotide having the formula



NI  
CON 4

wherein PM is a phosphate moiety, SM is a sugar moiety and BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, said PM being attached to SM, said BASE being attached to SM, and Sig being covalently attached to PM directly or via a chemical linkage, said Sig comprising a non-radioactive label moiety which can be directly or indirectly detected when attached to PM or when said modified nucleotide is incorporated into said oligo- or polynucleotide, or when said oligo- or polynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof, provided that when said oligo- or polynucleotide is an oligoribonucleotide or a polyribonucleotide, and when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2',3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide, wherein Sig comprises biotin, iminobiotin, an electron dense component, a magnetic component, a metal-containing component, a fluorescent component, a chemiluminescent component, a chromogenic component or a combination of any of the foregoing.

698. The oligo- or polynucleotide of claim 697, wherein said Sig is or renders the nucleotide or the oligo- or polynucleotide self-signaling or self-indicating or self-detecting.

Dean L. Engelhardt, et al.

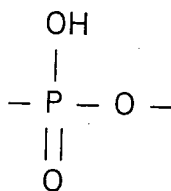
Serial No.: 08/479,997

Filed: June 7, 1995

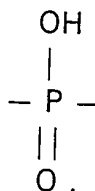
Page 32 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

<sup>117</sup>  
~~699~~. The oligo- or polynucleotide of claim ~~697~~<sup>116</sup>, wherein said Sig moiety comprises at least three carbon atoms.

<sup>118</sup>  
~~700~~. The oligo- or polynucleotide of claim ~~697~~<sup>116</sup>, wherein said covalent attachment is selected from the group consisting of



and



<sup>119</sup>  
~~701~~. The oligo- or polynucleotide of claim ~~697~~<sup>116</sup>, wherein said chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

<sup>120</sup>  
~~702~~. The oligo- or polynucleotide of claim ~~697~~<sup>116</sup>, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the  $\alpha$ -position relative to the point of attachment to the nucleotide, a  $-\text{CH}_2\text{NH}-$  moiety, or both.

<sup>121</sup>  
~~703~~. The oligo- or polynucleotide of claim ~~697~~<sup>116</sup>, wherein said chemical linkage comprises an allylamine group.

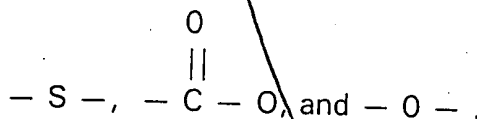
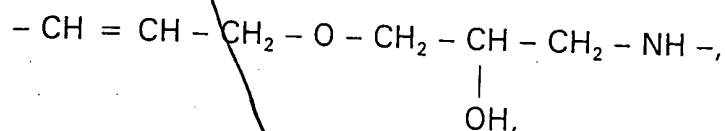
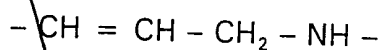
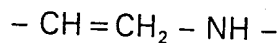
Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 33 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

704. The oligo- or polynucleotide of claim 697, wherein said chemical linkage comprises or includes an olefinic bond at the  $\alpha$ -position relative to the point of attachment to the nucleotide, or any of the moieties:



705. The oligo- or polynucleotide of claim 697, wherein said chemical linkage of Sig includes a glycosidic linkage moiety.

706. The oligo- or polynucleotide of claim 697, wherein said PM is a monophosphate, a diphosphate or a triphosphate and said Sig moiety is covalently attached to said PM through a phosphorus atom or a phosphate oxygen.

707. The oligo- or polynucleotide of claim 697, wherein said electron dense component comprises ferritin.

708. The oligo- or polynucleotide of claim 697, wherein said magnetic component comprises magnetic oxide.

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 34 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

<sup>127</sup>  
~~709~~. The oligo- or polynucleotide of claim ~~708~~<sup>126</sup>, wherein said magnetic oxide comprises ferric oxide.

<sup>128</sup>  
~~710~~. The oligo- or polynucleotide of claim ~~697~~<sup>116</sup>, wherein said metal-containing component is catalytic.

<sup>129</sup>  
~~711~~. The oligo- or polynucleotide of claim ~~697~~<sup>116</sup>, wherein said fluorescent component comprises a member selected from the group consisting of fluorescein, rhodamine and dansyl.

N1  
COD4. <sup>130</sup>  
~~712~~. The oligo- or polynucleotide of claim ~~697~~<sup>116</sup>, wherein said Sig moiety is attached to a terminal nucleotide in said oligo- or polynucleotide.

<sup>131</sup>  
~~713~~. The oligo- or polynucleotide of claim ~~712~~<sup>130</sup>, wherein the sugar moiety of said terminal nucleotide has a hydrogen atom at the 2' position thereof.

<sup>132</sup>  
~~714~~. The oligo- or polynucleotide of claim ~~712~~<sup>130</sup>, wherein the sugar moiety of said terminal nucleotide has an oxygen atom at each of the 2' and 3' positions thereof.

<sup>133</sup>  
~~715~~. The oligo- or polynucleotide of claim ~~697~~<sup>116</sup>, comprising at least one deoxyribonucleotide.



Dean L. Engelhardt, et al.

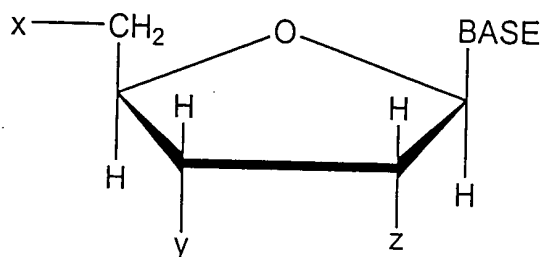
Serial No.: 08/479,997

Filed: June 7, 1995

Page 35 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

134

716. An oligo- or polynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polynucleotide comprising at least one modified nucleotide having the structural formula:



N<sup>1</sup>  
cont.  
wherein BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, and wherein BASE is attached to the 1' position of the pentose ring from the N1 position when BASE is a pyrimidine or from the N9 position when BASE is a purine or a deazapurine;

wherein x is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein y is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein z is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate; and

wherein Sig is covalently attached directly or through a chemical linkage to at least one phosphate selected from the group consisting of x, y and z, and a combination thereof, said Sig comprising a non-radioactive label moiety which can be directly or indirectly detected when so attached to said phosphate or when said modified nucleotide is incorporated into said oligo- or polynucleotide, or when said oligo- or polynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof, provided that when said oligo- or polynucleotide is an

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 36 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

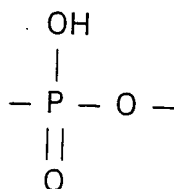
N<sup>1</sup>  
cov<sup>4</sup>.

oligoribonucleotide or a polyribonucleotide and when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2',3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide, wherein Sig comprises biotin, iminobiotin, an electron dense component, a magnetic component, a metal-containing component, a fluorescent component, a chemiluminescent component, a chromogenic component or a combination of any of the foregoing.

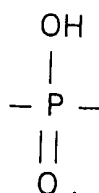
717. The oligo- or polynucleotide of claim 716, wherein said Sig is or renders the nucleotide or the oligo- or polynucleotide self-signaling or self-indicating or self-detecting.

<sup>135</sup>  
~~718.~~ The oligo- or polynucleotide of claim ~~716~~, wherein said Sig moiety comprises at least three carbon atoms.

<sup>134</sup>  
~~719.~~ The oligo- or polynucleotide of claim ~~716~~, wherein said covalent attachment is selected from the group consisting of



and



Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

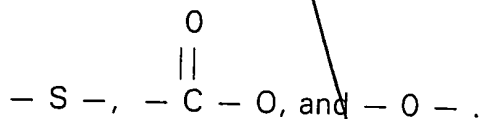
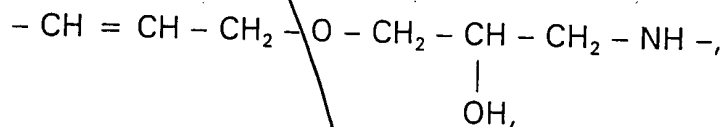
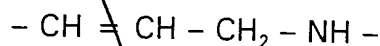
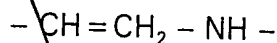
Page 37 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

<sup>137</sup>  
~~720.~~ The oligo- or polynucleotide of claim ~~716~~<sup>134</sup>, wherein said chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

SUB  
DIS  
N1  
CONT.  
721. The oligo- or polynucleotide of claim 716, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the  $\alpha$ -position relative to the point of attachment to the nucleotide, a  $-\text{CH}_2\text{NH}-$  moiety, or both.

<sup>134</sup>  
~~722.~~ The oligo- or polynucleotide of claim ~~716~~<sup>134</sup>, wherein said chemical linkage comprises an allylamine group.

723. The oligo- or polynucleotide of claim 716, wherein said chemical linkage comprises or includes an olefinic bond at the  $\alpha$ -position relative to x, y or z, or any of the moieties:



SUB  
DIS  
141  
~~724.~~ The oligo- or polynucleotide of claim ~~716~~<sup>134</sup>, wherein said chemical linkage of Sig includes a glycosidic linkage moiety.

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 38 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) – May 28, 2002]

<sup>142</sup>  
~~725~~. The oligo- or polynucleotide of claim ~~716~~<sup>134</sup>, wherein said x and y each  
comprise a member selected from the group consisting of a monophosphate, a  
diphosphate and a triphosphate and Sig moiety is covalently attached to either or  
both of said x and y through a phosphorus atom or a phosphate oxygen.

<sup>143</sup>  
~~726~~. The oligo- or polynucleotide of claim ~~716~~<sup>134</sup>, wherein said electron dense  
component comprises ferritin.

N!  
CDUx. <sup>144</sup>  
~~727~~. The oligo- or polynucleotide of claim ~~716~~<sup>134</sup>, wherein said magnetic component  
comprises magnetic oxide.

<sup>145</sup>  
~~728~~. The oligo- or polynucleotide of claim ~~727~~<sup>144</sup>, wherein said magnetic oxide  
comprises ferric oxide.

<sup>146</sup>  
~~729~~. The oligo- or polynucleotide of claim ~~716~~<sup>134</sup>, wherein said metal-containing  
component is catalytic.

<sup>147</sup>  
~~730~~. The oligo- or polynucleotide of claim ~~716~~<sup>134</sup>, wherein said fluorescent  
component comprises a member selected from the group consisting of fluorescein,  
rhodamine and dansyl.

<sup>148</sup>  
~~731~~. The oligo- or polynucleotide of claim ~~716~~<sup>134</sup>, wherein said Sig moiety is  
attached to a terminal nucleotide in said oligo- or polynucleotide.

<sup>149</sup>  
~~732~~. The oligo- or polynucleotide of claim ~~731~~<sup>148</sup>, wherein z of said terminal  
nucleotide comprises a hydrogen atom at the 2' position thereof.

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

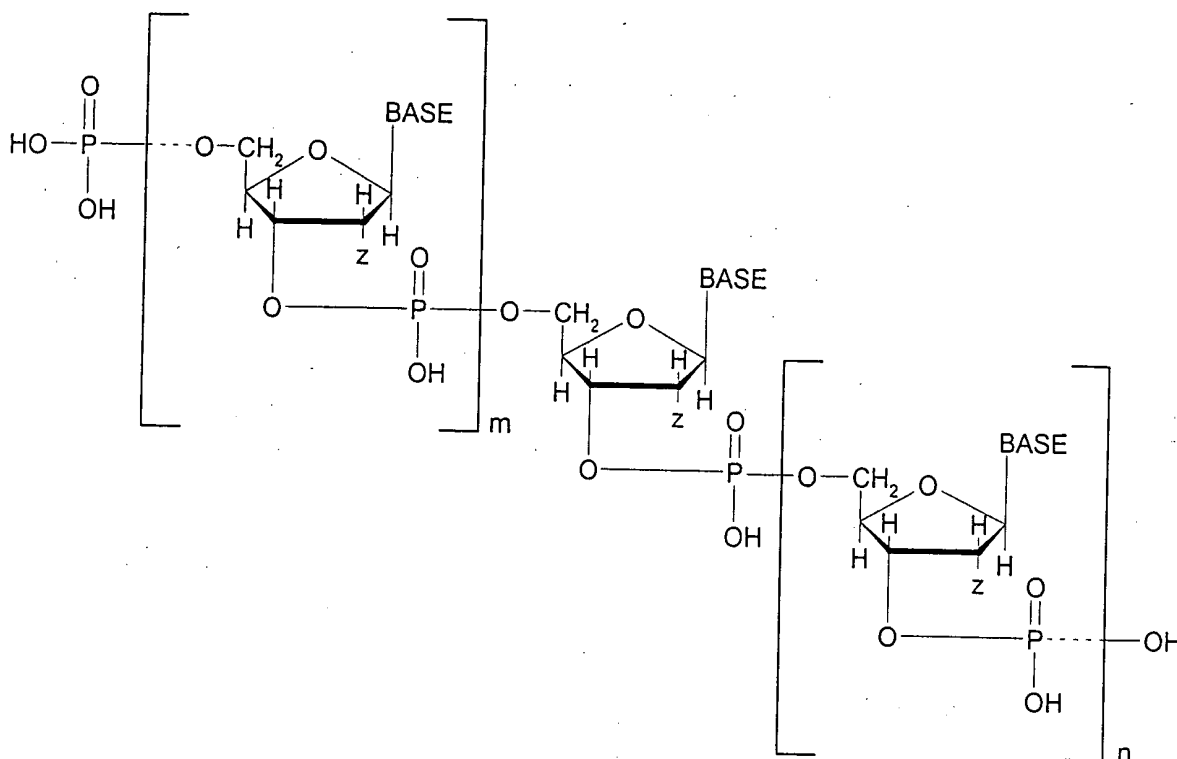
Filed: June 7, 1995

Page 39 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) – May 28, 2002]

<sup>150</sup>  
~~733~~. The oligo- or polynucleotide of claim ~~731~~<sup>148</sup>, wherein both y and z of said terminal nucleotide comprise an oxygen atom at each of the 3' and 2' positions thereof, respectively.

<sup>161</sup>  
~~734~~. The oligo- or polynucleotide of claim ~~716~~<sup>134</sup>, comprising at least one deoxyribonucleotide.

<sup>152</sup>  
~~735~~. The oligo- or polynucleotide of claim ~~716~~<sup>134</sup>, having the structural formula:



wherein m and n represent integers from 0 up to about 100,000, and wherein said Sig moiety is attached to at least one of the phosphate moieties in said structural formula.

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 40 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) – May 28, 2002]

SUB  
017

736. An oligo- or polydeoxyribonucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polydeoxyribonucleotide comprising at least one modified nucleotide having the formula

Sig-PM-SM-BASE

N<sup>1</sup>  
CON<sup>7</sup>

wherein PM is a phosphate moiety, SM is a sugar moiety and BASE is a base moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, said PM being attached to SM, said BASE being attached to SM, and Sig being covalently attached to PM through a chemical linkage comprising a polypeptide or a protein, and said Sig comprising a non-radioactive label moiety which can be directly detected when indirectly attached to PM through said polypeptide or protein chemical linkage or when said modified nucleotide is incorporated into said oligo- or polydeoxyribonucleotide or when said oligo- or polydeoxyribonucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof.

737. The oligo- or polydeoxyribonucleotide of claim 736, wherein said Sig is or renders the nucleotide or the oligo- or polydeoxyribonucleotide self-signaling or self-indicating or self-detecting.

154  
738. The oligo- or polydeoxyribonucleotide of claim 736, wherein said Sig moiety comprises at least three carbon atoms.

153

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

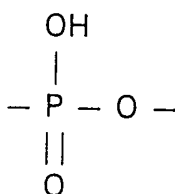
Filed: June 7, 1995

Page 41 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) – May 28, 2002]

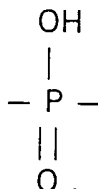
155

~~739.~~ The oligo- or polydeoxyribonucleotide of claim ~~736~~, wherein said covalent attachment is selected from the group consisting of

153



and



740. The oligo- or polydeoxyribonucleotide of claim 736, wherein said polypeptide or protein chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

741. The oligo- or polydeoxyribonucleotide of claim 736, wherein said PM is monophosphate, a diphosphate or a triphosphate and said Sig moiety is covalently attached via said polypeptide or protein chemical linkage to said PM through a phosphorus atom or phosphate oxygen.

158

~~742.~~ The oligo- or polydeoxyribonucleotide of claim ~~736~~, wherein Sig comprises a component selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, a metal-containing component, a fluorescent component, a chemiluminescent component, a chromogenic component or a combination of any of the foregoing.

153

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 42 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

<sup>159</sup>  
~~743.~~ The oligo- or polydeoxyribonucleotide of claim ~~742~~<sup>158</sup>, wherein said electron dense component comprises ferritin.

<sup>160</sup>  
~~744.~~ The oligo- or polydeoxyribonucleotide of claim ~~742~~<sup>158</sup>, wherein said magnetic component comprises magnetic oxide.

N!  
CONT.  
<sup>161</sup>  
~~745.~~ The oligo- or polydeoxyribonucleotide of claim ~~744~~<sup>160</sup>, wherein said magnetic oxide comprises ferric oxide.

<sup>162</sup>  
~~746.~~ The oligo- or polydeoxyribonucleotide of claim ~~742~~<sup>158</sup>, wherein said metal-containing component is catalytic.

<sup>163</sup>  
~~747.~~ The oligo- or polydeoxyribonucleotide of claim ~~742~~<sup>158</sup>, wherein said fluorescent component comprises a member selected from the group consisting of fluorescein, rhodamine and dansyl.

SUB  
019  
~~748.~~ The oligo- or polydeoxyribonucleotide of claim 736, wherein said oligo- or polydeoxyribonucleotide is terminally ligated or attached to said polypeptide or protein chemical linkage.

<sup>165</sup>  
~~749.~~ The oligo- or polydeoxyribonucleotide of claim ~~736~~<sup>153</sup>, wherein said polypeptide comprises polylysine.

<sup>166</sup>  
~~750.~~ The oligo- or polydeoxyribonucleotide of claim ~~736~~<sup>153</sup>, wherein said polypeptide is selected from the group consisting of avidin, streptavidin and anti-hapten immunoglobulin.



Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 43 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

SUB  
D20  
N1  
CONT.

~~751.~~ The oligo- or polydeoxyribonucleotide of claim ~~736~~, wherein said Sig moiety is attached via said polypeptide or protein chemical linkage to a phosphate moiety in a terminal nucleotide in said oligo- or polydeoxyribonucleotide.

~~168~~  
~~752.~~ The oligo- or polydeoxyribonucleotide of claim ~~751~~, wherein the sugar moiety of said terminal nucleotide has a hydrogen atom at the 2' position thereof.

~~169~~  
~~753.~~ The oligo- or polydeoxyribonucleotide of claim ~~751~~, wherein the sugar moiety of said terminal nucleotide has oxygen atoms at each of the 2' and 3' positions thereof.

~~170~~  
~~754.~~ The oligo- or polydeoxyribonucleotide of claim ~~736~~, comprising at least one ribonucleotide.

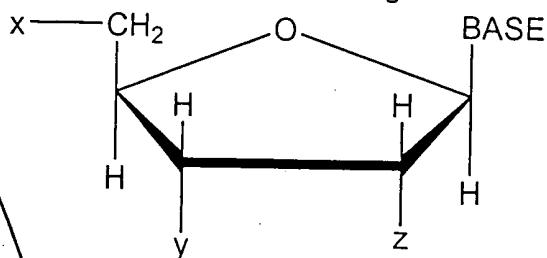
Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 44 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) – May 28, 2002]

755. An oligo- or polydeoxyribonucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polydeoxyribonucleotide comprising at least one modified nucleotide having the structural formula:



wherein BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, and wherein BASE is attached to the 1' position of the pentose ring from the N1 position when BASE is a pyrimidine or from the N9 position when BASE is a purine or a deazapurine;

wherein x is selected from the group consisting of  $\text{H}-$ ,  $\text{HO}-$ , a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein y is selected from the group consisting of  $\text{H}-$ ,  $\text{HO}-$ , a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein z is selected from the group consisting of  $\text{H}-$ ,  $\text{HO}-$ , a mono-phosphate, a di-phosphate and a tri-phosphate; and

wherein Sig is covalently attached through a chemical linkage to at least one phosphate selected from the group consisting of x, y, z, and a combination thereof, said chemical linkage comprising a polypeptide or a protein, and said Sig comprising a non-radioactive label moiety which can be directly or indirectly detected when attached to said phosphate via said polypeptide or protein chemical linkage or when said modified nucleotide is incorporated into said oligo- or polydeoxynucleotide or when said oligo- or polydeoxynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof.

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

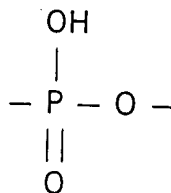
Filed: June 7, 1995

Page 45 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) – May 28, 2002]

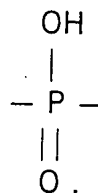
756. The oligo- or polydeoxyribonucleotide of claim 755, wherein said Sig is or renders the modified nucleotide or the oligo- or polydeoxyribonucleotide self-signaling or self-indicating or self-detecting.

172  
757. The oligo- or polydeoxyribonucleotide of claim 755, wherein said Sig moiety comprises at least three carbon atoms.

173  
758. The oligo- or polydeoxyribonucleotide of claim 755, wherein said covalent attachment is selected from the group consisting of



and



759. The oligo- or polydeoxyribonucleotide of claim 755, wherein said polypeptide or protein chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 46 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

SUB  
OAA  
CONT.

760. The oligo- or polydeoxyribonucleotide of claim 755, wherein said x and y each comprise a member selected from the group consisting of a monophosphate, a diphosphate and a triphosphate and said Sig moiety is covalently attached via said polypeptide or protein chemical linkage to either or both of said x and y a phosphorus atom or phosphate oxygen.

N1  
CONT.

<sup>176</sup>  
~~761~~. The oligo- or polydeoxyribonucleotide of claim 755, wherein Sig comprises a component selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, a metal-containing component, a fluorescent component, a chemiluminescent component, a chromogenic component, or a combination of any of the foregoing.

<sup>177</sup>  
~~762~~. The oligo- or polydeoxyribonucleotide of claim <sup>176</sup>~~761~~, wherein said electron dense component comprises ferritin.

<sup>178</sup>  
~~763~~. The oligo- or polydeoxyribonucleotide of claim <sup>176</sup>~~761~~, wherein said magnetic component comprises magnetic oxide.

<sup>179</sup>  
~~764~~. The oligo- or polydeoxyribonucleotide of claim <sup>178</sup>~~763~~, wherein said magnetic oxide comprises ferric oxide.

<sup>180</sup>  
~~765~~. The oligo- or polydeoxyribonucleotide of claim <sup>176</sup>~~761~~, wherein said metal-containing component is catalytic.

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 47 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) – May 28, 2002]

<sup>161</sup>  
~~766~~. The oligo- or polydeoxyribonucleotide of claim ~~761~~<sup>176</sup>, wherein said fluorescent component comprises a member selected from the group consisting of fluorescein, rhodamine and dansyl.

SUB  
D23  
  
NI  
CONT.  
  
~~767~~. The oligo- or polydeoxyribonucleotide of claim 755, wherein said oligo- or polydeoxyribonucleotide is terminally ligated or attached to said polypeptide or protein chemical linkage.

<sup>183</sup>  
~~768~~. The composition of claim ~~755~~<sup>171</sup>, wherein said polypeptide comprises polylysine.

<sup>184</sup>  
~~769~~. The composition of claim ~~755~~<sup>171</sup>, wherein said polypeptide is selected from the group consisting of avidin, streptavidin and anti-hapten immunoglobulin.

SUB  
D24  
  
~~770~~. The oligo- or polydeoxyribonucleotide of claim 755, wherein said Sig moiety is attached via said polypeptide or protein chemical linkage to a terminal nucleotide in said oligo- or polydeoxyribonucleotide.

<sup>186</sup>  
~~771~~. The oligo- or polydeoxyribonucleotide of claim ~~770~~<sup>185</sup>, wherein z of said terminal nucleotide comprises a hydrogen atom at the 2' position thereof.

<sup>187</sup>  
~~772~~. The oligo- or polydeoxyribonucleotide of claim ~~770~~<sup>185</sup>, wherein both y and z of said terminal nucleotide comprise an oxygen atom at each of the 3' and 2' positions thereof, respectively.

Dean L. Engelhardt, et al.

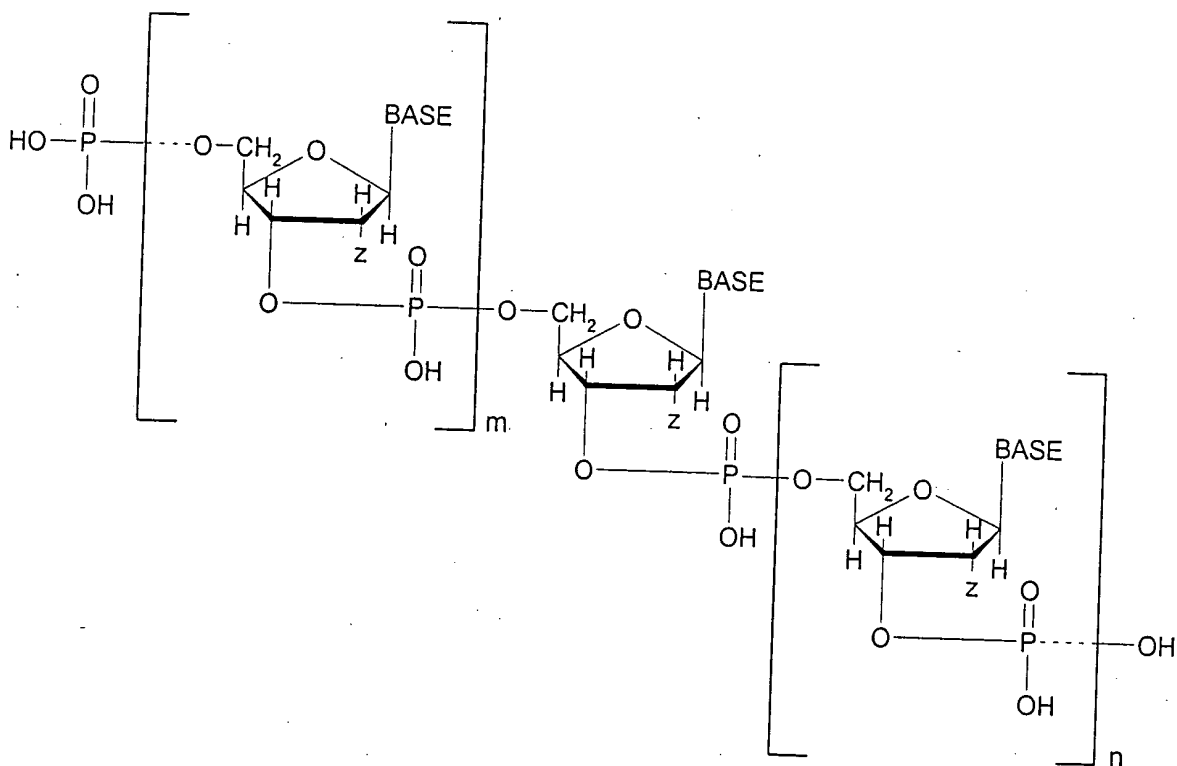
Serial No.: 08/479,997

Filed: June 7, 1995

Page 48 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

<sup>186</sup>  
~~773~~. The oligo- or polydeoxyribonucleotide of claim ~~755~~<sup>171</sup>, comprising at least one ribonucleotide.

<sup>189</sup>  
~~774~~. The oligo- or polydeoxyribonucleotide of claim ~~755~~<sup>171</sup>, having the structural formula:



wherein m and n represent integers from 0 up to about 100,000, and wherein said Sig moiety is attached to at least one of the phosphate moieties in said structural formula.

Dean L. Engelhardt, et al.

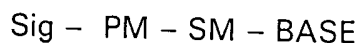
Serial No.: 08/479,997

Filed: June 7, 1995

Page 49 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

SUB  
D25

775. An oligo- or polynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polynucleotide comprising at least one modified nucleotide having the formula



N<sup>1</sup>  
CON<sup>4</sup>.

wherein PM is a phosphate moiety, SM is a sugar moiety and BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, said PM being attached to SM, said BASE being attached to SM, and Sig being covalently attached to PM via a chemical linkage comprising a polypeptide or a protein, said Sig comprising a non-radioactive label moiety which can be directly or indirectly detected when attached to PM via said polypeptide or protein chemical linkage or when said modified nucleotide is incorporated into said oligo- or polynucleotide, or when said oligo- or polynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof, provided that when said oligo- or polynucleotide is an oligoribonucleotide or a polyribonucleotide, and when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2',3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide.

776. The oligo- or polynucleotide of claim 775, wherein said Sig is or renders the nucleotide or the oligo- or polynucleotide self-signaling or self-indicating or self-detecting.

191  
777. The oligo- or polynucleotide of claim 775, wherein said Sig moiety comprises at least three carbon atoms.

190  
775.

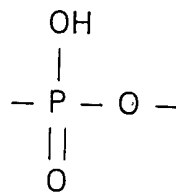
Dean L. Engelhardt, et al.

Serial No.: 08/479,997

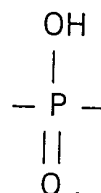
Filed: June 7, 1995

Page 50 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

<sup>192</sup>  
~~778~~. The oligo- or polynucleotide of claim ~~775~~<sup>190</sup>, wherein said covalent attachment is selected from the group consisting of



and



<sup>N'</sup>  
<sup>CON</sup>  
779. The oligo- or polynucleotide of claim 775, wherein said polypeptide or protein chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

<sup>SUB</sup>  
<sup>026</sup>  
780. The oligo- or polynucleotide of claim 775, wherein said PM is a monophosphate, a diphosphate or a triphosphate and said Sig moiety is covalently attached via said polypeptide or protein chemical linkage to said PM through a phosphorus atom or a phosphate oxygen.

<sup>195</sup>  
~~781~~. The oligo- or polynucleotide of claim ~~775~~<sup>190</sup>, wherein Sig comprises a component selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, a metal-containing component, a fluorescent component, a chemiluminescent component, a chromogenic component or a combination of any of the foregoing.



Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 51 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

<sup>196</sup>  
~~782~~. The oligo- or polynucleotide of claim ~~781~~<sup>195</sup>, wherein said electron dense component comprises ferritin.

<sup>147</sup>  
~~783~~. The oligo- or polynucleotide of claim ~~781~~<sup>195</sup>, wherein said magnetic component comprises magnetic oxide.

<sup>198</sup>  
~~784~~. The oligo- or polynucleotide of claim ~~783~~<sup>197</sup>, wherein said magnetic oxide comprises ferric oxide.

<sup>199</sup>  
~~785~~. The oligo- or polynucleotide of claim ~~781~~<sup>195</sup>, wherein said metal-containing component is catalytic.

<sup>200</sup>  
~~786~~. The oligo- or polynucleotide of claim ~~781~~<sup>195</sup>, wherein said fluorescent component comprises a member selected from the group consisting of fluorescein, rhodamine and dansyl.

~~787~~. The oligo- or polynucleotide of claim 775, wherein said oligo- or polynucleotide is terminally ligated or attached to said polypeptide or protein chemical linkage.

<sup>202</sup>  
~~788~~. The oligo- or polynucleotide of claim ~~775~~<sup>190</sup>, wherein said polypeptide comprises polylysine.

<sup>203</sup>  
~~789~~. The oligo- or polynucleotide of claim ~~775~~<sup>190</sup>, wherein said polypeptide is selected from the group consisting of avidin, streptavidin and anti-hapten immunoglobulin.

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 52 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

SW3  
028  
N<sup>1</sup>  
COU<sup>1</sup>.

790. The oligo- or polynucleotide of claim 775, wherein said Sig moiety is attached via said polypeptide or protein chemical linkage to a terminal nucleotide in said oligo- or polynucleotide.

205  
204  
791. The oligo- or polynucleotide of claim ~~790~~, wherein the sugar moiety of said terminal nucleotide has a hydrogen atom at the 2' position thereof.

206  
204  
792. The oligo- or polynucleotide of claim ~~790~~, wherein the sugar moiety of said terminal nucleotide has an oxygen atom at each of the 2' and 3' positions thereof.

207  
190  
793. The oligo- or polynucleotide of claim ~~775~~, comprising at least one deoxyribonucleotide.

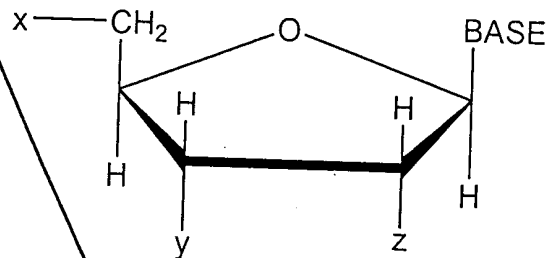
Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 53 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) – May 28, 2002]

794. An oligo- or polynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polynucleotide comprising at least one modified nucleotide having the structural formula:



N<sup>1</sup>  
COU<sup>4</sup>

wherein BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, and wherein BASE is attached to the 1' position of the pentose ring from the N1 position when BASE is a pyrimidine or from the N9 position when BASE is a purine or a deazapurine;

wherein x is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein y is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein z is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate; and

wherein Sig is covalently attached through a chemical linkage to at least one phosphate selected from the group consisting of x, y and z, and a combination thereof, said chemical linkage comprising a polypeptide or a protein, and said Sig comprising a non-radioactive label moiety which can be directly detected when attached to said phosphate via said polypeptide or protein chemical linkage or when said modified nucleotide is incorporated into said oligo- or polynucleotide, or when said oligo- or polynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof, provided that when said oligo- or polynucleotide is an

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 54 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

SUB  
025  
CO24

oligoribonucleotide or a polyribonucleotide and when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2',3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide.

N<sup>1</sup>  
CO24

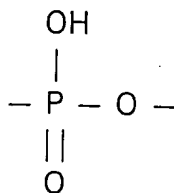
795. The oligo- or polynucleotide of claim 794, wherein said Sig is or renders the nucleotide or the oligo- or polynucleotide self-signaling or self-indicating or self-detecting.

209 208

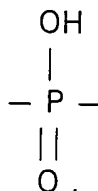
796. The oligo- or polynucleotide of claim 794, wherein said Sig moiety comprises at least three carbon atoms.

210 208

797. The oligo- or polynucleotide of claim 794, wherein said covalent attachment is selected from the group consisting of



and



SUB  
030

798. The oligo- or polynucleotide of claim 794, wherein said polypeptide or protein chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 55 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

SUB  
O3D  
COU<sup>1</sup>

799. The oligo- or polynucleotide of claim 794, wherein said x and y each comprise a member selected from the group consisting of a monophosphate, a diphosphate and a triphosphate and Sig moiety is covalently attached to either or both of said x and y a phosphorus atom or a phosphate oxygen.

213

2108

800. The oligo- or polynucleotide of claim 794, wherein Sig comprises a component selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, a metal-containing component, a fluorescent component, a chemiluminescent component, a chromogenic component or a combination of any of the foregoing.

N<sup>1</sup>  
COU<sup>1</sup>

214

213

801. The oligo- or polynucleotide of claim 800, wherein said electron dense component comprises ferritin.

215

213

802. The oligo- or polynucleotide of claim 800, wherein said magnetic component comprises magnetic oxide.

216

215

803. The oligo- or polynucleotide of claim 802, wherein said magnetic oxide comprises ferric oxide.

217

213

804. The oligo- or polynucleotide of claim 800, wherein said metal-containing component is catalytic.

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 56 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

<sup>218</sup>  
~~805.~~ The oligo- or polynucleotide of claim ~~800~~<sup>213</sup>, wherein said fluorescent component comprises a member selected from the group consisting of fluorescein, rhodamine and dansyl.

SUB  
031  
  
N<sup>1</sup>  
COUT.  
  
~~806.~~ The oligo- or polynucleotide of claim 794, wherein said oligo- or polynucleotide is terminally ligated or attached to said polypeptide or protein chemical linkage.

<sup>220</sup>  
~~807.~~ The oligo- or polynucleotide of claim ~~794~~<sup>208</sup>, wherein said polypeptide comprises polylysine.

<sup>221</sup>  
~~808.~~ The oligo- or polynucleotide of claim ~~794~~<sup>208</sup>, wherein said polypeptide is selected from the group consisting of avidin, streptavidin and anti-hapten immunoglobulin.

SUB  
032  
  
~~809.~~ The oligo- or polynucleotide of claim 794, wherein said Sig moiety is attached via said polypeptide or protein chemical linkage to a terminal nucleotide in said oligo- or polynucleotide.

<sup>223</sup>  
~~810.~~ The oligo- or polynucleotide of claim ~~809~~<sup>222</sup>, wherein z of said terminal nucleotide comprises a hydrogen atom at the 2' position thereof.

<sup>224</sup>  
~~811.~~ The oligo- or polynucleotide of claim ~~809~~<sup>222</sup>, wherein both y and z of said terminal nucleotide comprise an oxygen atom at each of the 3' and 2' positions thereof, respectively.

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 57 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

225

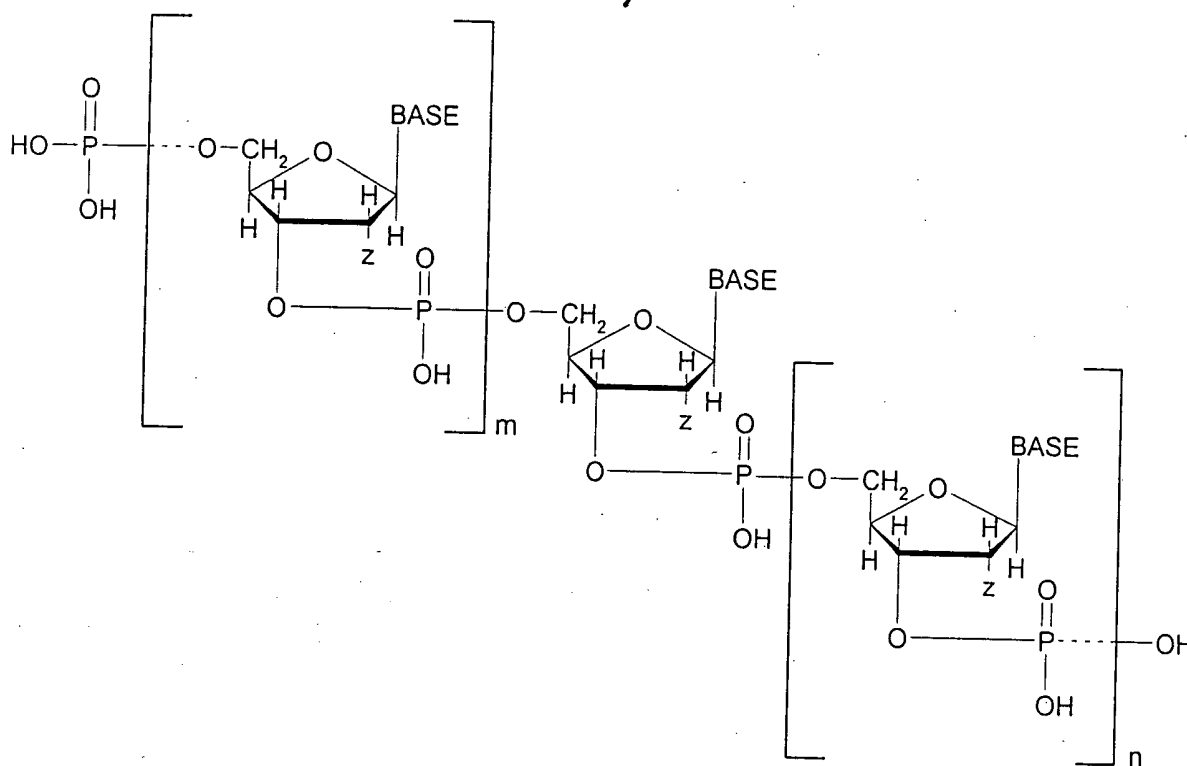
208

~~812.~~ The oligo- or polynucleotide of claim ~~794~~, comprising at least one deoxyribonucleotide.

226

208

~~813.~~ The oligo- or polynucleotide of claim ~~794~~, having the structural formula:



wherein m and n represent integers from 0 up to about 100,000, and wherein said Sig moiety is attached to at least one of the phosphate moieties in said structural formula.

~~814.~~ The oligo- or polydeoxyribonucleotide of claims 454 or 658, wherein said Sig is covalently attached to PM through a chemical linkage comprising a polypeptide or a protein.

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 58 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

228

227

~~815.~~ The oligo- or polydeoxyribonucleotide of claim ~~814~~, wherein said polypeptide comprises polylysine.

SUB  
034

~~816.~~ The oligo- or polydeoxyribonucleotide of claim 814, wherein said polypeptide or protein is selected from the group consisting of avidin, streptavidin and anti-hapten immunoglobulin.

230

20 97

~~817.~~ The oligo- or polydeoxyribonucleotide of claims ~~586~~ or ~~677~~, wherein said Sig is covalently attached to said at least one phosphate through a chemical linkage comprising a polypeptide or a protein.

N'  
COND.

231

230

~~818.~~ The oligo- or polydeoxyribonucleotide of claim ~~817~~, wherein said polypeptide comprises polylysine.

232

~~819.~~ The oligo- or polydeoxyribonucleotide of claim 817, wherein said polypeptide or protein is selected from the group consisting of avidin, streptavidin and anti-hapten immunoglobulin.

SUB  
035

233

~~820.~~ The oligo- or polynucleotide of claims 617 or 697, wherein said Sig is covalently attached to PM via a chemical linkage comprising a polypeptide or a protein.

234

233

~~821.~~ The oligo- or polydeoxyribonucleotide of claim ~~820~~, wherein said polypeptide comprises polylysine.



Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

Page 59 [Reply Under 37 C.F.R. §1.111 (In Response To The  
November 26, 2001 Office Action) - May 28, 2002]

SUB  
036  
822. The oligo- or polydeoxyribonucleotide of claim 820, wherein said polypeptide or protein is selected from the group consisting of avidin, streptavidin and anti-hapten immunoglobulin.

N'  
CDV7.  
823. The oligo- or polynucleotide of claims 637 or 716, wherein said Sig is covalently attached to said at least one phosphate through a chemical linkage comprising a polypeptide or a protein.

237  
824. The oligo- or polydeoxyribonucleotide of claim 823, wherein said polypeptide comprises polylysine. 236

SUB  
037  
825. The oligo- or polydeoxyribonucleotide of claim 824, wherein said polypeptide or protein is selected from the group consisting of avidin, streptavidin and anti-hapten immunoglobulin.

✓  
Cancel claims 454-567.

\* \* \* \* \*